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## **REMARKS**

### **Amendments**

Claims 1-32 have been canceled. Claims 33-46 have been added. The newly added claims do not add or constitute new matter. Support for the newly added claims may be found throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, 33-46 are pending in the instant application.

### **Objections**

The Examiner has objected to claim 1 because the abbreviation BSMAP is not spelled out at the first occurrence of the term. Applicant has canceled claim 1, and the newly added claims spell out the term “brain-specific membrane anchored protein” at its first occurrence, claim 33.

Claims 5-7 have also been objected to by the Examiner because they encompass non-elected embodiments, *e.g.* cells comprising a disruption in a BSMAP gene that are not necessarily derived from a non-human transgenic animal. Claims 5-7 have been canceled, and Applicant submits that none of newly added claims 33-46 are drawn to cells not obtained from the claimed transgenic mouse.

### **Rejections**

#### ***Rejection under 35 U.S.C. § 101***

The Examiner has rejected claims 1-12, 15, 17-26 and 30 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either an asserted utility which is specific and substantial, or a well established utility. Applicant respectfully traverses this rejection.

The Examiner has based the rejection on the alleged lack of a useful phenotype exhibited by the transgenic mice of the present invention. The Examiner has concluded that the observed difference in prepulse inhibition between the transgenic mice comprising homozygous disruption of the BSMAP gene and wild-type mice is not statistically significant. This conclusion is

apparently based upon error bars in Figure 3 of the prepulse inhibition values for wild-type mice, which the Examiner states “extend to and include the mean prepulse inhibition values for the transgenic knockout mouse”. The Examiner states that since there is no other teaching in the specification or known in the art related to the function of the BSMAP gene, the claimed invention has no utility which is specific and substantial.

The Applicant disagrees with the Examiner’s conclusions, and traverses the rejection. As a first issue, the Applicant is not aware of any standard of statistical significance of a phenotype required for the establishment of patentability (utility) of a transgenic mouse. If such a standard exists, it is respectfully requested that the Examiner make the Applicant aware of the standard. Further, even if such a standard exists, Applicant clearly disclosed in the instant application that a statistically significant difference was observed between the transgenic mice and wild-type mice (see Page 51, line 29 through Page 60, line 2 of the specification). Applicant submits that this difference does exist. And finally, with regard to the error bars, Applicant notes that the presence of overlapping error bars does not necessarily establish or support a lack of statistical significance, as asserted by the Examiner.

As the Applicant has canceled claims 1-12, 15, 17-26 and 30, this rejection no longer applies to these claims.

The Applicant submitted new claims 33-46, which relate to a transgenic mouse whose genome comprises a disruption in the mouse BSMAP gene, which when homozygous leads to a phenotype of increased prepulse inhibition relative to a wild-type mouse, to methods of making and using the mouse, to cells derived from the mouse, and to targeting constructs and methods of producing targeting constructs used to produce the mouse.

Applicant submits that the transgenic mouse as recited in claims 33-46 is supported by an asserted specific and substantial utility. More particularly, the transgenic mice have been established to exhibit significantly increased prepulse inhibition. Prepulse inhibition, at the time of filing, was known in the art and taught by the instant specification to be associated with schizophrenia. As such, the transgenic mouse as claimed would be supported by a variety of utilities, such as, for example, the investigation into and/or discovery of therapeutic agents related to schizophrenia or as an animal model related to schizophrenia.

Applicant requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 101 in light of the amendments to the claims and arguments set forth above.

***Rejection under 35 U.S.C. § 112, first paragraph - Enablement***

The Examiner has rejected claims 1-12, 15, 17-26 and 30 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant respectfully traverses this rejection.

In one aspect, the Examiner has alleged that one skilled in the art would not know how to use the claimed invention as of the filing date because it is allegedly not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above. In light of the cancellation of claims and the remarks set forth above (in response to the utility rejection under 35 U.S.C. § 101), Applicant submits that this aspect of the enablement rejection under 35 U.S.C. § 112, first paragraph is no longer relevant, and requests its withdrawal. As noted above, the pending claims are supported by a specific and substantial asserted utility or a well established utility..

In another aspect of this rejection, the Examiner claims that the specification is not enabling for these claims, drawn to a construct targeting a BSMAP gene **derived from any animal species**, a method for producing the same targeting construct, for **any non-human transgenic animal** including a transgenic mouse comprising a disruption in a BSMAP gene **having any phenotype** including a stimulus processing abnormality or prepulse inhibition abnormality, a cell derived from the same transgenic animal, a method of producing a transgenic mouse comprising a disruption in BSMAP gene by introducing the targeting construct of the present invention **into any cell**, and methods for identifying an agent that modulates the expression or the function of a BSMAP gene or ameliorates a phenotype associated with a disruption in a BSMAP gene using the non-human transgenic animal of the present invention. This aspect of the rejection is based on the unpredictability of phenotypes in transgenic mice, the limitation of ES cell technology to the mouse system, and alleged lack of guidance in the specification and art with regard to the novel BSMAP gene, in light of the scope of the claims.

The Applicant traverses the rejection. However, claims 1-12, 15, 17-26 and 30 have been canceled.

New claims 33-46 are drawn to a transgenic mouse whose genome comprises a homozygous disruption in endogenous mouse BSMAP gene, wherein the transgenic mouse exhibits increased prepulse inhibition, methods of producing the mouse, methods of using the

mouse to screen for agents, mouse cells comprising the disruption, and to a targeting construct and method of producing the targeting construct for producing the disruption in a mouse.

The Applicant submits that the enablement rejection as it applies to newly added claims 33-46 has been overcome in light of the amendments and remarks contained in this response, specifically in that the claims 1) recite a transgenic **mouse** whose genome comprises a **homozygous** disruption of the **mouse** BSMAP gene; 2) recite a phenotype of increased prepulse inhibition, supported by the specification (see above); 3) recite use of a **mouse embryonic stem cell** to produce the disruption in the transgenic mouse; and 4) relate to a targeting construct for disruption mouse BSMAP gene in a mouse. The Applicant submits that one skilled in the art would be able to **make and use** the invention as recited in claims 33-46. Therefore, the rejection under 35 U.S.C. § 112, first paragraph, for enablement is no longer relevant. Applicant respectfully requests withdrawal of the rejection.

***Rejection under 35 U.S.C. § 112, first paragraph – Written Description***

The Examiner has rejected claims 1-5, 8-9, 11-12 and 15 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Applicant respectfully traverses the rejection.

Claims 1-5, 8-9, 11-12 and 15 are drawn to a targeting construct for a BSMAP gene, a method for producing such a targeting construct, a non-human transgenic animal comprising a disruption in a BSMAP gene and a cell derived from the same, as well as methods for identifying an agent that modulates the function or expression of a BSMAP gene using the non-human transgenic animal. It appears the basis for the written description rejection is the scope of the claims, which the Examiner states encompass BSMAP genes derived from any non-human animal and further encompass any non-human animal comprising a disruption in any BSMAP gene.

The Applicant has canceled claims 1-5, 8-9, 11-12 and 15, rendering the written description rejection moot. New claims 33-46 have been submitted, which no longer recite any non-human transgenic animal or any BSMAP gene. The Applicant submits that the specification describes the subject matter of these claims in such a way as to convey possession of the invention in accordance with the written description provision of 35 U.S.C. § 112, first

paragraph. Therefore, the Applicant respectfully requests withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph.

In view of the cancellation of claims and arguments set forth above, the rejections under 35 U.S.C. § 112, first paragraph, with regard to enablement and written description, are no longer relevant. The Applicant submits that new claims 33-46 fully meet the requirements and are patentable under 35 U.S.C. § 112, first paragraph.

***Rejection under 35 U.S.C. § 112, second paragraph***

The Examiner rejected claims 10 and 21-23 under 35 U.S.C. § 112, second paragraph, for being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully traverses this rejection.

Specifically, the Examiner asserts that the claims are unclear in their recitation of the term “the cell” in step(s) (b). The Examiner questions whether the cell referred to is the cell containing the BS MAP gene targeting construct or the cell without the gene targeting construct. The Applicant disagrees that the term renders the claims indefinite, but in order to expedite prosecution of the instant application, the claim has been cancelled, rendering the rejection moot.

New claims 33-46 particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph. More particularly, these claims no longer recite the term “the cell” in a way that is unclear or indefinite. Therefore, the Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

In light of the amendments to the claims and remarks set forth above, it is believed that the claims are currently in condition for allowance. Notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-227.

Respectfully submitted,

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